

A novel score in the prediction of rhythm outcome after ablation of atrial fibrillation: The SUCCESS score

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ABSTRACT

Objective: The aim of the present study was to assess the predictive value of the CHADS₂, CHA₂DS₂-VASc, R₂CHADS₂, and APPLE scores for rhythm outcome in patients with atrial fibrillation (AF) after catheter ablation.

Methods: The cohort of the present study consisted of 192 patients with AF who underwent a total of 265 ablations. Rhythm outcome was documented between 3 and 24 month after ablation. The mentioned scores were calculated for every patient.

Results: Of the patients, 139 (72%) were successfully treated having freedom of any atrial tachyarrhythmia, whereas 21 (11%) had partial success, and 32 (17%) had failure. For univariate analysis, the APPLE score was the only significant predictor of outcome after ablation with an odds ratio (OR) of 1.485 [95% confidence interval (CI) 1.075–2.052, p-value 0.017]. A multivariate binary regression corrected for possible confounders showed that the APPLE score (OR 1.527, 95% CI 1.082–2.153, p-value 0.016) along with the number of previous ablations (OR 5.831, 95% CI 1.356–25.066, p-value 0.018) is a significant predictor of outcome. A novel score (SUCCESS) was created by adding one point to the APPLE score for each previously performed ablation. This novel score demonstrated an improvement in receiver operating characteristic curve analysis (area under the curve 0.657 vs. 0.620). However, these findings were not significant in our study (p-value 0.219).

Conclusion: Both the APPLE and the novel SUCCESS scores are superior to the CHADS₂, CHA₂DS₂-VASc, and R₂CHADS₂ scores in predicting AF recurrence after catheter ablation. The SUCCESS score appears to have a higher predictive value than the APPLE score and might be a valuable tool to estimate the risk of AF recurrence in patients eligible for catheter ablation. (*Anatol J Cardiol* 2019; 21: 00-00)

Keywords: catheter ablation, predictor, CHA₂DS₂-VASc, recurrence

Introduction

Atrial fibrillation (AF) is the most common type of arrhythmia, affecting >1% of all adults worldwide and causing a significant impact on public health (1, 2). Over the last decades, catheter ablation has become an established form of treatment, especially in patients where medical therapy is not sufficient for rhythm stabilization or not tolerated due to side effects (3). Treatment often includes anticoagulation therapy owing to an increased risk of stroke or systemic embolic events in patients with AF (4, 5). Well-established score systems (CHADS₂, CHA₂DS₂-VASc, and R₂CHADS₂) are commonly used to estimate the risk of cardioembolic events (6-8).

Few studies have aimed to assess these score systems and/or other risk factors, such as enlargement of the left atrium (LA), to predict rhythm outcome after catheter ablation (9–12). However, these studies showed inconsistent results when it came to

reproducing a similar significant predictive value of the studied scores. Hence, there are currently no strong recommendations suggesting the use of CHADS₂ or CHA₂DS₂-VASc score rather than other score systems (13, 14).

The aim of the present study was to assess which risk factors and score systems have a predictive value for the rhythm outcome after catheter ablation in our patient cohort of a single tertiary care center in Switzerland. The study focuses primarily on four different score systems (CHADS₂, CHA₂DS₂-VASc, R₂CHADS₂, and APPLE score) and secondarily on the specific components of those scores independently.

Methods

Study population

All patients suffering from symptomatic AF (either paroxysmal or persistent) undergoing one or multiple catheter ablations at our institution between June 2009 and February 2014 were in-

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cluded in the study. In accordance with the current guidelines, paroxysmal AF was defined as episodes terminating within 7 days, whereas persistent AF was defined as lasting >7 days (15). Data, including sex, age, type of AF, number of previous ablations, history of congestive heart failure, hypertension, diabetes mellitus, history of stroke or transient ischemic attack (TIA), coronary artery disease (CAD), size of the LA, ejection fraction (EF) of the left ventricle, structural heart disease, creatinine blood level, height, and weight, on comorbidities and risk factors were collected in all patients.

Scores

The following data were used to calculate different scores: CHADS₂ score (1 point for congestive heart failure, hypertension, age ≥75 years, and diabetes mellitus and 2 points for history of stroke or TIA; range from 0 to 6) (6), CHA₂DS₂-VASc score (1 point for congestive heart failure, hypertension, age 65–74 years, diabetes mellitus, vascular disease, and female sex and 2 points for age ≥75 years and history of stroke or TIA; range from 0 to 10) (7), R₂CHADS₂ score (CHADS₂ score plus an additional 2 points for creatinine clearance [estimated glomerular filtration rate (eGFR)] <60 mL/min; range from 0 to 8) (8), APPLE score (1 point for age >65 years, persistent AF, eGFR <60 mL/min/1.73 m², LA diameter ≥43 mm, and left ventricular EF <50%; range from 0 to 5) (13), and eGFR was estimated using the MDRD-Study-Formula: $eGFR = 175 * \text{serum creatinine}^{-1.154} * \text{Age}^{-0.203} * [1.210 \text{ if black}] * [0.742 \text{ if female}]$. However, the factor 1.210 was not applied because the race of the patients was not part of the registered data in the present study (16).

Ablation

Radiofrequency (RF) energy was used for catheter ablation in most cases. Only in a few cases was an alternative source of energy used (cryoenergy, n=6 and laser light, n=2). The technique used in all patients consisted of a wide-area circumferential point-by-point RF ablation of the ipsilateral pulmonary veins ostia. The acute success was confirmed by the achievement of the procedural endpoint that consisted in electrical isolation of all pulmonary veins from the LA. This was demonstrated by circular mapping of each pulmonary vein showing the entrance and exit block. Additional linear lesions or substrate modifications were performed at the discretion of the operator in patients suffering from persistent AF (17–21).

Definition of success

After the last follow-up, patients were divided into three groups based on their outcome. “Success” was defined as lack of AF lasting >30 s in Holter electrocardiographies (ECGs) and absence of arrhythmia symptoms. “Partial success” was defined as reduction of AF duration >90% in patients without clinically symptomatic AF. This definition is based mainly on Holter ECGs and was included because even though these patients do not meet the criteria of the “success” category, they do not

qualify for another ablation. “Failure” was defined as any result not meeting the criteria of the previous two groups, representing recurrence of AF. Antiarrhythmic drugs were used after the intervention if required at the discretion of the treating physician. However, the use of antiarrhythmic drugs was not taken into consideration for the definition of success.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD) or median with interquartile ranges and were compared using the Student’s t-test or Mann-Whitney U test as appropriate. Categorical data are presented as frequency (percentages) and were compared using the Fisher’s exact or chi-square test. Variables with a significant odds ratio (OR) (p<0.05) in a univariate analysis model for the prediction of the primary outcome were included in an Enter-Method multivariate logistic regression model to determine independent predictors of the studied outcome. Calibration was determined by the Hosmer–Lemeshow goodness-of-fit test. For discrimination, the C statistics and receiver operating characteristic (ROC) curves were constructed to assess and compare the ability of the CHADS₂, CHA₂DS₂-VASc, R₂CHADS₂, APPLE, and SUCCESS scores for the prediction of the recurrence of AF. All probability values and confidence intervals (CIs) were two-sided. A p-value of <0.05 was considered significant, a p-value of <0.1 and >0.05 was considered a trend, and all tests were two-tailed. All statistical analyses were performed using SPSS version 23.0 software (SPSS Inc., Chicago, IL, USA).

Ethical standards

The Local Ethics Committee approved the study in accordance with the ethical standards of the Declaration of Helsinki.

Results

Patient characteristics

The cohort of the present study consisted of 192 patients undergoing a total of 265 catheter ablations. A single procedure was performed in 128 (67%) patients, and multiple procedures were performed in 64 (33%) patients, with 9 (5%) patients requiring a total of three ablations. The mean number of procedures per patient was 1.38±0.57. Of the patients, 146 (76%) were men, and 46 (24%) were women. Out of the 192 patients, 116 (60%) were diagnosed with paroxysmal AF, whereas 76 (40%) were diagnosed with persistent AF. The mean age at the time of the procedure was 61.8±9.2 years, and the mean time between first diagnosis and ablation was 5.8±4.3 years. All ablations were performed between 2009 and 2014. Table 1 summarizes the patient characteristics and risk factors. Table 2 shows the distribution within the different score systems.

Follow-up

Follow-up examinations were performed at 3, 6, 12, and 24 months, which included symptom assessment and ECG monitor-

Table 1. Patient characteristics

Characteristics		
No. of patients	192	
No. of ablations	265	
Ablations per patient	1.37±0.58	
Patients with one ablation	128	66.67%
Patients with two ablations	55	28.65%
Patients with three ablations	9	4.69%
Time to procedure (years)	5.81±4.33	
Male	146	76.04%
Female	46	23.96%
Age (years)	61.8±9.19	
Paroxysmal AF	116	60.42%
Persistent AF	76	39.58%
Risk factors		
Previous procedures	64	33.33%
Heart failure	10	5.21%
Hypertension	92	47.92%
Age 65–74 years	64	33.33%
Age >74 years	16	8.33%
Diabetes mellitus	16	8.33%
History of stroke/TIA	20	10.42%
CAD	20	10.42%
LA size (mm)	43.7±6.86	
LA size >42 mm	103	53.65%
EF (%)	58.5±8.06	
EF <50%	22	11.46%
Structural heart disease	13	6.77%
Creatinine (µmol/L)	91.7±18.20	
eGFR (mL/min/1.73 m ²)	71.3±16.84	
Renal dysfunction	52	27.08%
Weight (kg)	85.9±15.97	
Height (cm)	176.0±9.14	
BMI (kg/m ²)	27.7±4.23	

AF – atrial fibrillation; BMI – body mass index; CAD – coronary artery disease; eGFR – estimated glomerular filtration rate; EF – ejection fraction; LA – left atrium; TIA – transient ischemic attack

ing. These findings were used for evaluating the success of the treatment of each patient.

In 83% of the patients, Holter ECGs were available during follow-up. For the remaining patients, outcome was evaluated by ECG recordings and symptom assessment. The mean follow-up duration was 19 (SD±12; range 3–55) months, with 142 (74%) patients being assessed at least 12 months and 70 (36%) patients at least 24 months after the procedure.

Table 2. Scores

CHADS ₂ score		
0 point	77	40.10%
1 point	75	39.06%
2 points	23	11.98%
3 points	15	7.81%
4 points	2	1.04%
Mean±SD	0.91±0.96	
CHA ₂ DS ₂ -VASc score		
0 point	51	26.56%
1 point	46	23.96%
2 points	43	22.40%
3 points	28	14.58%
4 points	17	8.85%
5 points	6	3.13%
6 points	1	0.52%
Mean±SD	1.67±1.44	
R ₂ CHADS ₂ score		
0 point	64	33.33%
1 point	46	23.96%
2 points	30	15.63%
3 points	41	21.35%
4 points	7	3.65%
5 points	3	1.56%
6 points	1	0.52%
Mean±SD	1.45±1.36	
APPLE score		
0 point	32	16.67%
1 point	54	28.13%
2 points	59	30.73%
3 points	30	15.63%
4 points	14	7.29%
5 points	3	1.56%
Mean±SD	1.73±1.21	
SUCCESS score		
0 point	27	14.06%
1 point	40	20.83%
2 points	54	28.13%
3 points	39	20.31%
4 points	19	9.90%
5 points	13	6.77%
Mean±SD	2.11±1.41	

Rhythm outcome

Out of all 192 cases, 139 (72%) were classified as “success”, 21 (11%) as “partial success”, and 32 (17%) as “failure”, leading to a total of 160 (83%) patients being treated “successfully” or at least “partial successfully”. A subgroup analysis was performed

for the 70 (36%) patients who were followed up for at least 24 months after the procedure. In this subgroup, 41 (59%) patients were in paroxysmal AF, and 29 (41%) patients were in persistent AF. Of the cases, 43 (61%) were classified as “success”, 16 (23%) as “partial success”, and 11 (16%) as “failure”. In conclusion, 59 (84%) out of the 70 cases were considered a “success” or “partial success” after a follow-up of 2 years.

During the duration of our study, 3 (1.6%) patients showed left atrial flutter. All three patients returned to sinus rhythm either spontaneously (one case) or after electrical cardioversion (two cases). All other arrhythmia recurrences were AF. Early recurrence AF within the 3-month blanking period was not considered.

Predictors for recurrence of AF after catheter ablation

During the follow-up period, 32 (17%) patients showed recurrence of AF. The primary results showed that there was no

significantly higher incidence or prevalence of heart failure, hypertension, diabetes mellitus, or CAD in patients with AF recurrence than in those with normal sinus rhythm. However, a trend was observable for persistent AF (p-value 0.068), LA size (0.068), time to procedure (0.066), and previous ablations (0.098) (Table 3).

Of the different scores, only the APPLE score demonstrated a significant predictive value for recurrence of AF in the univariate logistic regression analysis (OR 1.485, 95% CI 1.075–2.052, p-value 0.017), whereas the CHADS₂, CHA₂D₂-VASc, and R₂CHADS₂ scores were all not significant predictors for rhythm outcome (Table 4).

The APPLE score also showed a better predictive value using the ROC curve analysis [area under the curve (AUC) 0.620, p-value 0.040] than CHADS₂ (AUC 0.535, p-value 0.548), CHA₂D₂-VASc (AUC 0.542, p-value 0.472) and R₂CHADS₂ (AUC 0.570, p-

Table 3. Predictors of atrial fibrillation

Variables	Study population n=192	Arrhythmia recurrences		P-value
		No (n=160)	Yes (n=32)	
Age (years)	61.77±9.188	61.7±9.1	62.1±9.8	0.848
Males (%)	76	76.7	72.4	0.640
Heart failure (%)	5.2	4.9	6.9	0.649
Persistent AF (%)	39.6	36.8	55.2	0.068
Hypertension (%)	47.9	47.2	51.7	0.691
Diabetes (%)	8.3	9.2	3.4	0.474
History of stroke/TIA (%)	10.4	10.4	10.3	1.000
CAD (%)	10.4	9.8	13.8	0.513
LA size >42 mm (%)	53.6	50.9	69	0.105
LA size (mm)	43.67±6.8	43.3±6.8	45.9±6.8	0.068
EF <50% (%)	11.5	10.4	17.2	0.339
EF (%)	58.52±8.06	58.7±7.5	57.3±10.9	0.420
SHD (%)	7.3	6.6	11.1	0.419
Creatinine (µmol/L)	91.74±18	91.1±17.2	95.1±22.8	0.279
eGFR <60 mL/min/1.73 m ² (%)	27.1	25.2	37.9	0.175
eGFR (mL/min/1.73 m ²)	71.25±16.8	71.8±16.9	68.3±16.8	0.306
Previous ablation (%)	33.3	31.3	44.8	0.199
BMI (kg/m ²)	27.67±4.23	27.6±4.4	27.8±3.5	0.844
Time to procedure (years)	5.81±4.3	5.6±4.3	7.2±4.5	0.066
Total ablations	1.38±0.57	1.3±0.5	1.6±0.7	0.098
CHADS ₂ score	0.91±0.96	0.9±1.0	0.9±0.8	0.881
CHA ₂ D ₂ -VASc score	1.67±1.43	1.6±1.5	1.8±1.3	0.608
R ₂ CHADS ₂ score	1.45±1.86	1.4±1.4	1.7±1.3	0.302
APPLE score	1.73±1.2	1.6±1.7	2.2±1.4	0.014

AF – atrial fibrillation; BMI – body mass index; CAD – coronary artery disease; eGFR – estimated glomerular filtration rate; EF – ejection fraction; LA – left atrium; TIA – transient ischemic attack; SHD - structural heart disease

Scores	OR	95% CI	P-value
LA size (mm)	1.056	0.995-1.120	0.071
EF (%)	0.980	0.934-1.029	0.419
Persistent AF	2.113	0.951-4.693	0.066
eGFR (mL/min/1.73 m ²)	0.987	0.963-1.012	0.305
Time to procedure (years)	1.082	0.994-1.179	0.070
Previous ablations	1.917	1.030-3.569	0.040
CHADS ₂ score	1.032	0.686-1.552	0.880
CHA ₂ DS ₂ -VASc score	1.074	0.819-1.407	0.607
R ₂ CHADS ₂ score	1.160	0.876-1.536	0.301
APPLE score	1.485	1.075-2.052	0.017

AF – atrial fibrillation; eGFR – estimated glomerular filtration rate; EF – ejection fraction; LA – left atrium; OR – odds ratio

value 0.228). Nevertheless, the difference in AUC did not reach statistical significance (p-value >0.05) (Fig. 1).

The distribution of the cohort within the APPLE score for 0, 1, 2, and ≥3 points was 17%, 28%, 31%, and 24%, respectively. The rates for AF recurrence for these subgroups were 6% (APPLE score 0), 15% (1), 14% (2), and 31% (≥3) (p=0.227) (Fig. 2). The risks (OR) for recurrence of AF were 2.609 (95% CI 0.518–13.133, p=0.245) (APPLE score 1), 2.353 (95% CI 0.469–11.816, p=0.299) (APPLE score 2), and 4.583 (95% CI 0.942–22.310, p=0.059) (APPLE score ≥3) compared with a score of 0.

After this initial analysis, we performed a multivariate analysis, including the APPLE score and the two risk factors with the highest significance from the logistic regression analysis that were previous ablations (OR 1.917, 95% CI 1.030–3.569, p-value 0.040) and time to procedure (OR 1.082, 95% CI 0.994–1.179, p-value 0.070). In this analysis, both the APPLE score (OR 1.527,

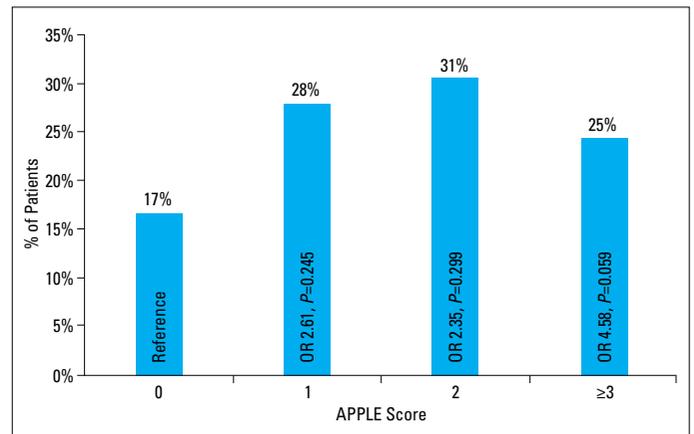


Figure 2. APPLE score distribution. Distribution and risk for atrial fibrillation recurrence of study cohort. OR - odds ratio

95% CI 1.082–2.153, p-value 0.016) and previous ablations ≥2 (OR 5.831, 95% CI 1.356–25.066, p-value 0.018) remained significant. We also generated a multivariate binary regression model corrected for three significant confounding variables with an appropriate fit (H and L test: chi-square 4.039, p-value 0.854).

These findings showed that the number of previous ablations appears to have a significant impact on the rhythm outcome. In order to confirm this observation, we created a new score system based on the APPLE score by adding a point for every previous ablation. We called this novel score SUCCESS [Severity of AF type (persistent AF), Unsuccessful previous ablations (1 point per ablation), Creatinine Clearance (eGFR <60 mL/min/1.73 m²), Elderly (>65 years), Size of LA (≥43 mm), Systolic left ventricular EF (<50%)].

We compared those two score systems using the ROC curve analysis. The newly formed SUCCESS score demonstrated an improvement (AUC 0.657) compared with the APPLE score (AUC 0.620), which was not significant however (p-value 0.219) (Fig. 3). Furthermore, the SUCCESS score remained a significant predictor

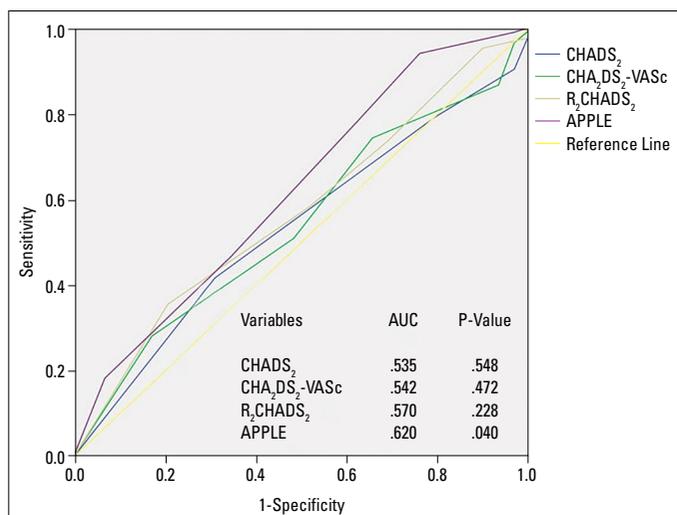


Figure 1. ROC curve 1. Prediction of outcome for CHADS₂, CHA₂DS₂-VASc, R₂CHADS₂, and APPLE scores

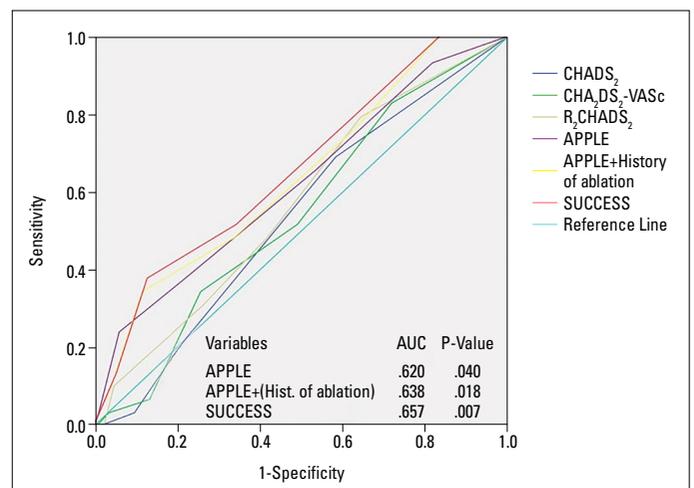


Figure 3. ROC curve 2. Comparison between all scores including “APPLE+ (history of ablation)” (max. 1 additional point) and “SUCCESS” (1 additional point for each previous ablation)

of recurrence despite the addition of partial success to recurrence [outcome of recurrence including partial success: OR 1.453 (95% CI 1.146–1.843), p-value 0.002 and outcome of recurrence excluding partial success: OR 1.539 (95% CI 1.145–2.051), p-value 0.003].

Discussion

To the best of our knowledge, this is the first study comparing the predictive value for rhythm outcome after catheter ablation in patients with AF of all four scores CHADS₂, CHA₂DS₂-VASc, R₂CHADS₂, and APPLE. Among these score systems, only the APPLE score was a significant predictor for rhythm outcome in our patient cohort. The newly introduced SUCCESS score might predict outcome even better.

The most recently reported APPLE scoring system by Kornej et al. (13) showed to be capable of predicting rhythm outcome in patients after first and repeated ablation procedures and has proven to be superior to the previously reported scoring systems (22). In our study, we obtained very similar results to those by Kornej et al. (13) who introduced the novel APPLE score. Using the ROC curve analysis, we received an AUC of 0.620 [Kornej et al. (13): 0.634]. The distribution of patients within the APPLE score of the two cohorts was comparable (APPLE scores of 0, 1, 2, and ≥3: 17%, 28%, 31%, and 25%, respectively) [Kornej et al. (13): 21%, 34%, 31%, and 25%, respectively], as was the risk (OR) for arrhythmia recurrence [APPLE scores of 1, 2, or ≥3: 2.61 (95% CI 0.52–3.13), 2.35 (95% CI 0.47–11.81), and 5.58 (95% CI 0.94–22.31), respectively] [Kornej et al. (13): 1.73 (95% CI 1.17–2.55), 2.79 (95% CI 1.90–4.12), and 4.70 (95% CI 3.03–7.30), respectively]. While Kornej et al. (13) demonstrated the predictive value of the APPLE score in patients undergoing their first ablation and also for repeated ablations (22), they did not include previous interventions as a factor in their score. We sought to further improve the predictive value of this score by awarding an additional point for every previously performed ablation in the patient's medical history, which was the most significant specific risk factor in our study. This newly created SUCCESS score performed slightly better in the ROC curve analysis than the APPLE score (AUC 0.657 vs. 0.620) (Fig. 3). However, this improvement did not reach statistical significance (p-value 0.219). This might be due to the low number of AF recurrences [32] in our cohort of 192 patients. The predictive value of the SUCCESS score proposed in the present study certainly needs to be tested in a larger cohort.

Previously, several studies evaluated predictors for rhythm outcome after catheter ablation in patients with AF. For the specific risk factors, a meta-analysis found that the most significant variables were persistent AF, valvular AF, size of LA >50 mm, and recurrence of AF within 30 days (11). However, the two most significant specific risk factors of our results (previous ablations and time to procedure) were not analyzed in this meta-analysis. A recent study reported that a shorter period between diagnosis and ablation of AF increases the rate of success of the procedure (23).

The predictive value of the number of previous ablations for prediction rhythm outcome in patients with AF has not been evaluated yet. However, there are data available comparing the success rates of first-time ablations and repeated ablations. In contrast to our findings, data suggest that these success rates remain unchanged, independently of the total count of ablations (14), or that they increase with each additional procedure (24, 25).

CHADS₂ and CHA₂DS₂-VASc scores are the two most extensively studied scores. Both are primarily used to determine the usefulness of anticoagulation in patients with AF. Although they appear to be associated with recurrence after ablations as proposed by multiple studies, their predictive value is, however, modest (9, 12, 14, 25, 26). Fewer studies have evaluated the role of novel scores, such as the R₂CHADS₂ score, which was created to assess the risk of stroke and systemic embolism in patients with AF (8). R₂CHADS₂ appeared to have a better predictive value than the CHADS₂ and CHA₂DS₂-VASc score systems (9).

We did not include other scoring systems because they either had no predictive value for rhythm outcome [HATCH (27, 28)], included early recurrence and therefore were unpractical for baseline prediction [BASE-AF (29) and MB-Later (30)] or were used for patients who underwent repeated ablations [ALARMEc (31)].

Since the SUCCESS score is mainly based on the existing APPLE score, it also shares its advantages (13). Its composition is based on the results of a multivariate analysis of a cohort of 2067 patients (9). Combining the significant, independent predictors of AF recurrence of that study (persistent AF, renal insufficiency, age, size of LA, and reduced EF) with our own results (previous number of ablation procedure) results in a score system, which is easy to use and consists of parameters routinely assessed in patients, making it convenient for clinical practice. Further studies with larger cohorts should be conducted to confirm our findings.

Study limitations

This was a single-center cohort. The main limitation of the present study is the small number of patients, which is not sufficient to establish a novel scoring system on its own. However, we suggest that by adding an additional point for previously performed ablations to the APPLE score might improve its predictive value and should be tested in larger cohorts. Furthermore, as arrhythmia recurrences might be underdetected, further studies with continuous rhythm monitoring are needed to confirm these findings.

Conclusion

Both the APPLE and the novel SUCCESS scores are superior to the CHADS₂, CHA₂DS₂-VASc, and R₂CHADS₂ scores in predicting the recurrence of atrial tachyarrhythmia after catheter ablation in patients with AF. The SUCCESS score appears to have a higher predictive value than the APPLE score. Further studies with larger number of patients should be performed to confirm our findings.

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Peer-review: Externally peer-reviewed.

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